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Original Research Article

DIAGNOSTIC ACCURACY OF SERUM CYSTATIN C COMPARED TO SERUM CREATININE FOR DETECTION OF HEPATORENAL DYSFUNCTION IN PATIENTS WITH DECOMPENSATED CHRONIC LIVER DISEASE: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Hepatorenal dysfunction is a serious complication of decompensated chronic liver disease (DCLD) associated with poor prognosis and increased mortality. This prospective observational study aimed to evaluate the diagnostic accuracy of serum Cystatin C compared to serum creatinine for detecting hepatorenal dysfunction and assessing renal function using estimated glomerular filtration rate (eGFR). A total of 50 patients with DCLD were included, with a mean age of 48.72 ± 8.30 years and male predominance (76%). Hepatorenal dysfunction was present in 60% of patients. Serum creatinine levels were elevated (>2 mg/dL) in 52% of patients, with a sensitivity of 83.33%, specificity of 100%, and diagnostic accuracy of 90%. In contrast, serum Cystatin C levels were elevated (>1.3 mg/L) in 66% of patients and demonstrated superior diagnostic performance, with 100% sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy. Receiver operating characteristic curve analysis showed a higher area under the curve for serum Cystatin C (0.997) compared to serum creatinine (0.917), indicating superior diagnostic accuracy. Cystatin C-based eGFR also showed higher diagnostic accuracy compared to creatinine-based eGFR. Hepatorenal dysfunction was significantly associated with worsening liver disease severity, lower serum albumin levels, and higher bilirubin, prothrombin time, and INR levels. These findings suggest that serum Cystatin C is a more sensitive and reliable biomarker than serum creatinine for detecting renal dysfunction in patients with decompensated chronic liver disease and may be useful for early diagnosis and improved clinical management.

Keywords: Cystatin C; Serum creatinine; Hepatorenal dysfunction; Decompensated chronic liver disease.

INTRODUCTION

Cirrhosis represents the final stage of chronic liver injury and remains a leading cause of global morbidity and mortality. In 2019, cirrhosis accounted for approximately 2.4% of all deaths worldwide, underscoring its significant public health impact.[1] The epidemiology of cirrhosis is evolving due to improved control of hepatitis B and hepatitis C infections, alongside rising rates of alcohol use and metabolic risk factors such as obesity and non-alcoholic fatty liver disease.[2]

India bears a substantial burden of chronic liver disease, contributing significantly to global liver-related mortality.[3] Cirrhosis and other chronic liver diseases account for a considerable proportion of deaths nationally, with alcohol, viral hepatitis, and metabolic liver disease being the predominant etiologies.[4] Notably, liver-related mortality demonstrates a marked male predominance.[1]

Anatomically, cirrhosis is defined as a diffuse hepatic process characterized by fibrosis and regenerative nodule formation resulting from sustained liver injury.[5] Clinically, cirrhosis progresses through compensated and decompensated stages. Compensated cirrhosis may remain asymptomatic despite advanced fibrosis. Decompensated chronic liver disease (DCLD) is characterized by complications such as ascites, variceal haemorrhage, hepatic encephalopathy, or hepatorenal syndrome.[6] The first episode of decompensation represents a critical prognostic milestone, with median survival declining from approximately 10–12 years in compensated disease to nearly 1–2 years following decompensation.[6]

Among the complications of decompensated cirrhosis, hepatorenal dysfunction is one of the most severe and life-threatening. Hepatorenal syndrome (HRS) is defined as functional renal failure occurring in advanced liver disease in the absence of structural kidney injury.[7] It results from profound circulatory dysfunction characterized by splanchnic vasodilatation, activation of endogenous vasoconstrictor systems, and progressive renal hypoperfusion.[8] The International Club of Ascites (ICA) has refined the diagnostic criteria for HRS, emphasizing dynamic changes in serum creatinine and the exclusion of intrinsic renal disease.[9]

Early identification of renal dysfunction in cirrhosis is essential because even minor deterioration in kidney function significantly worsens prognosis. Serum creatinine is traditionally used to estimate glomerular filtration rate (GFR); however, in cirrhotic patients, it may underestimate renal impairment due to reduced hepatic creatine synthesis, sarcopenia, increased volume of distribution, and analytical interference from hyperbilirubinemia.[10] These limitations may delay recognition of acute kidney injury and HRS.

Cystatin C has emerged as a promising alternative biomarker of renal function. It is a low molecular weight protein produced at a constant rate by all nucleated cells and freely filtered by the glomeruli. Unlike creatinine, its serum concentration is minimally influenced by muscle mass or dietary factors. Recent studies suggest that serum Cystatin C may provide a more sensitive assessment of early renal dysfunction in patients with cirrhosis and ascites, and elevated levels have been associated with increased mortality.[11]

Given the high morbidity and mortality associated with hepatorenal dysfunction in DCLD, there is a need for more reliable biomarkers that enable earlier detection of renal impairment. Therefore, this study aims to evaluate the prevalence and etiological profile of hepatorenal dysfunction in patients with decompensated chronic liver disease and to assess the diagnostic performance of serum Cystatin C in comparison with serum creatinine for early detection of renal impairment.

MATERIALS AND METHODS

2.1. Study Design and Setting

This prospective observational study was conducted in the Department of General Medicine at Mahatma Gandhi Memorial Government Hospital, Tiruchirappalli, over a period of one year from February 2024 to January 2025.

2.2. Study Population

The study included adult patients admitted with decompensated chronic liver disease (DCLD). Decompensated cirrhosis was defined as cirrhosis associated with one or more decompensating events, including jaundice, ascites, hepatic encephalopathy, hepatorenal syndrome, or variceal haemorrhage**.**

2.3. Inclusion and Exclusion Criteria

Patients aged 18–65 years with DCLD of any etiology who provided informed consent were included. Patients with known pre-existing renal disease, renal transplant, immunocompromised state, prior history of hepatorenal syndrome, recent nephrotoxic drug intake, or unwillingness to participate were excluded

2.4. Sample Size and Sampling Technique

The sample size was calculated using a prevalence of 27% based on Cystatin C–based eGFR progression reported by Gottlieb et al., with a 95% confidence level (Z = 1.96), absolute precision of 13%, and a 10% non-response rate. The final calculated sample size was 50 participants. Consecutive sampling was employed, and eligible patients admitted during the study period were enrolled until the required sample size was achieved.

2.5. Data Collection

Data were collected using a semi-structured questionnaire, clinical examination, and laboratory Demographic characteristics, clinical features, and etiological factors were recorded. Patients were evaluated for complications, including ascites, hepatic encephalopathy, upper gastrointestinal bleeding, spontaneous bacterial peritonitis, coagulopathy, and hepatorenal dysfunction. Baseline laboratory investigations included serum total bilirubin, serum albumin, prothrombin time (PT), international normalized ratio (INR), serum creatinine, serum Cystatin C, and renal profile Somatostatin or vasoactive medications were not administered within one week prior to blood sampling. Kidney impairment was assessed according to the KDIGO 2024 Clinical Practice Guidelines for Chronic Kidney Disease and Acute Kidney Injury

2.6. Operational Definitions

Hepatorenal dysfunction was defined using the following cut-off values:

- Serum creatinine >2 mg/dL
- Serum Cystatin C >1.3 mg/L

Serum creatinine-based estimated glomerular filtration rate (eGFR) was calculated using the MDRD equation:

$$GFR = 175 \times (S.Cr)^{-1.234} \times (Age)^{-0.179} \times 0.79 \text{ (if female)}$$

Cystatin C–based eGFR was calculated as:

$$GFR = 78.64 \times (CystatinC)^{-0.964}$$

2.7. Laboratory Methods

Serum total bilirubin and albumin were measured using the Labospect 008 fully automated analyzer (Hitachi, Japan) with kits from Sichuan Maccura Biotechnology Co., Ltd. Prothrombin time was assessed using the CS-5100 automated coagulation analyzer (Sysmex, Japan) with Siemens Healthcare Diagnostics kits. Serum creatinine and Cystatin C were measured using the Labospect 008 analyzer (Hitachi, Japan). The detection ranges were 0.13–7.80 mg/L for Cystatin C and 7.1–8840 µmol/L for serum creatinine

2.8. Variables

Dependent variables included serum Cystatin C levels and serum creatinine levels. Independent variables included age, gender, etiology of liver disease, and complications such as hepatic encephalopathy, coagulopathy, and spontaneous bacterial peritonitis

2.9. Statistical Analysis

Data were entered in Microsoft Excel 2019 and analysed using SPSS version 21. Descriptive statistics were used to summarize demographic and clinical characteristics. Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequencies and percentages. Associations between renal biomarkers and hepatorenal dysfunction were assessed using appropriate inferential statistical tests. Receiver operating characteristic (ROC) curve analysis was performed to determine the diagnostic performance of serum creatinine, serum Cystatin C, and their respective eGFR values.

RESULTS AND DISCUSSION

Patient Demographics and Clinical Characteristics

Results. Fifty patients with decompensated chronic liver disease were enrolled in this prospective observational study. The cohort was predominantly male (76%, n=38) with a mean age of 48.72±8.30 years (range 35-70 years). According to Child-Pugh classification, 74% (n=37) were classified as Class B and 26% (n=13) as Class C, indicating predominantly advanced but not end-stage disease. Alcohol-related liver disease was the predominant etiology (56%), followed by viral hepatitis (10%), autoimmune hepatitis (10%), cryptogenic/NASH (8%), PBC/PSC (8%), and other causes including vascular and metabolic disorders (8%).

The predominance of alcohol-related liver disease (56%) in our cohort is consistent with global epidemiological patterns, where alcohol accounts for 32-43% of cirrhosis cases, with regional variation depending on alcohol consumption patterns and public health interventions.[1,2] The relatively lower prevalence of viral hepatitis (10%) compared to some Asian studies reflects improved hepatitis B vaccination coverage and increased access to direct-acting antiviral agents for hepatitis C in recent years.[3] The 8% prevalence of cryptogenic/NASH mirrors the rising global burden of metabolic-associated fatty liver disease concurrent with the obesity and diabetes epidemics.[4] The male predominance (76%) aligns with established epidemiological data showing that men account for approximately two-thirds of liver-related deaths globally, likely reflecting higher rates of alcohol consumption and occupational exposures in male populations.[5]

Prevalence and Severity of Hepatorenal Dysfunction

Hepatorenal dysfunction was present in 60% of patients (n=30), representing the most prevalent renal complication. Other complications included ascites (52%, n=26), hepatic encephalopathy (26%, n=13), coagulopathy (26%, n=13), upper gastrointestinal bleeding (18%, n=9), and spontaneous bacterial peritonitis (14%, n=7). Notably, all Child-Pugh Class C patients (100%, n=13) demonstrated hepatorenal dysfunction, compared to only 45.9% (17/37) of Class B patients (p=0.001), demonstrating a strong correlation between disease severity and renal impairment. Patients with hepatorenal dysfunction exhibited significantly worse hepatic synthetic function, with lower serum albumin (2.68±0.35 vs. 2.97±0.10 g/dL, p=0.001), higher total bilirubin (3.33±1.14 vs. 2.65±0.16 mg/dL, p=0.001), prolonged prothrombin time (6.20±1.03 vs. 5.25±0.44 seconds, p=0.012), and elevated INR (2.22±0.28 vs. 1.94±0.16, p<0.001) compared to those without this complication. [Table 1]

Table 1: Laboratory Parameters in Patients with and Without Hepatorenal Dysfunction

Parameter	HRD Present (n=30)	HRD Absent (n=20)
Serum albumin, g/dL	2.68 ± 0.35**	2.97 ± 0.10
Total bilirubin, mg/dL	3.33 ± 1.14**	2.65 ± 0.16
Prothrombin time, sec	6.20 ± 1.03*	5.25 ± 0.44
INR	2.22 ± 0.28**	1.94 ± 0.16

*Data presented as mean ± SD. HRD, hepatorenal dysfunction; INR, international normalized ratio. *p<0.05, **p<0.001 vs. HRD absent group.*

The 60% prevalence of hepatorenal dysfunction in our cohort reflects the advanced stage of disease, with universal involvement in Child-Pugh Class C patients, indicating that renal impairment is an inevitable complication of end-stage cirrhosis. This finding aligns with the established pathophysiology in which portal hypertension induces progressive splanchnic vasodilation, reducing effective arterial

blood volume despite increased cardiac output.[6,7] The body's compensatory activation of vasoconstrictor systems—including the renin-angiotensin-aldosterone system, sympathetic nervous system, and arginine vasopressin—initially maintains systemic blood pressure and renal perfusion. However, as the disease progresses, these compensatory mechanisms become overwhelmed, resulting in intense renal vasoconstriction, decreased glomerular filtration, and ultimately hepatorenal syndrome.8 The strong association between hepatorenal dysfunction and markers of impaired hepatic synthetic function (lower albumin, higher bilirubin, prolonged coagulation parameters) underscores the systemic nature of hepatic decompensation and suggests that renal impairment is not merely a consequence of hemodynamic changes but also reflects the broader metabolic and inflammatory derangements characteristic of advanced liver disease.[9]

Comparative Performance of Renal Biomarkers

Mean serum creatinine was 2.55±1.09 mg/dL (range: 1.2-4.8 mg/dL) with 52% of patients (n=26) exceeding 2 mg/dL (Figure 1A). Mean cystatin C was 2.44±1.44 mg/L (range: 0.70-4.70 mg/L), with 66% of patients (n=33) demonstrating elevated levels >1.3 mg/L (Figure 1B). The distribution of cystatin C showed a distinct bimodal pattern, clearly separating patients with and without hepatorenal dysfunction. Creatinine-based eGFR (calculated using the MDRD formula) yielded a mean of 32.64±28.96 mL/min/1.73m² (range: 10.22-67.56 mL/min/1.73m²) (Figure 2A), while cystatin C-based eGFR demonstrated a significantly higher mean of 112.70±75.37 mL/min/1.73m² (range: 39.37-246.81 mL/min/1.73m²) (Figure 2B), representing a threefold discrepancy between the two estimation methods.

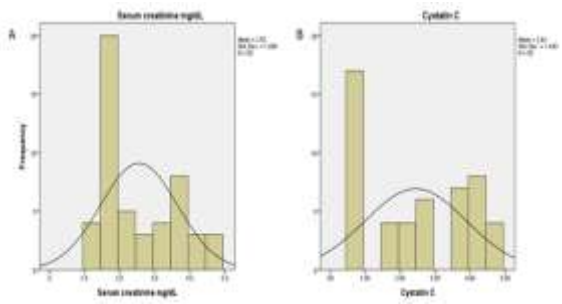

Figure 1. Distribution of renal biomarkers. (A) Serum creatinine distribution showing mean of 2.55 mg/dL with 52% of patients exceeding the 2 mg/dL threshold commonly used to define renal impairment. (B) Cystatin C distribution demonstrating mean of 2.44 mg/L with distinct bimodal pattern reflecting clear separation between patients with and without hepatorenal dysfunction at the 1.3 mg/L cutoff.

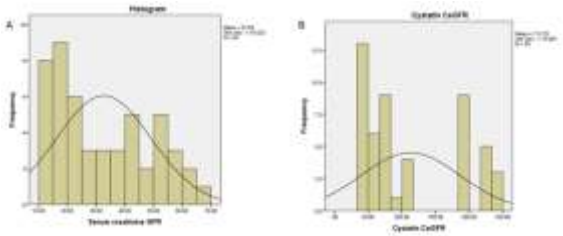

Figure 2. Distribution of estimated glomerular filtration rate. (A) Creatinine-based eGFR showing mean of 32.64 mL/min/1.73m² with majority of patients demonstrating significantly reduced renal function. (B) Cystatin C-based eGFR with mean of 112.70 mL/min/1.73m², demonstrating substantially higher estimated values and suggesting that creatinine-based formulas significantly underestimate true GFR in cirrhotic patients due to reduced muscle mass and altered hepatic creatine metabolism.

The threefold discrepancy between creatinine-based eGFR (32.64 mL/min/1.73m²) and cystatin C-based eGFR (112.70 mL/min/1.73m²) confirms that creatinine substantially underestimates renal function in cirrhotic patients, consistent with findings from multiple international studie.[10,11] This underestimation occurs because creatinine is a breakdown product of creatine phosphate in skeletal muscle, and cirrhotic patients typically exhibit severe sarcopenia (muscle wasting), resulting in reduced creatinine production independent of renal function. Additionally, hepatic synthesis of creatine is impaired in liver disease, further reducing the creatinine pool. The increased volume of distribution from ascites and edema dilutes serum creatinine concentrations, while elevated bilirubin can interfere with colorimetric creatinine assays, leading to falsely low values.[12,13] In contrast, cystatin C is a 13-kDa cysteine proteinase inhibitor produced at constant rates by all nucleated cells, is freely filtered by glomeruli, and is nearly completely reabsorbed and catabolized by proximal tubular cells. Critically, its production is independent of muscle mass, age, gender, hepatic synthesis, and nutritional status, making it a more reliable marker of GFR in cirrhotic patients.[14,15] The distinct bimodal distribution of cystatin C in our cohort, with clear separation at 1.3 mg/L, further supports its utility as a discriminatory biomarker for hepatorenal dysfunction.

Diagnostic Accuracy for Detecting Hepatorenal Dysfunction

Serum creatinine >2 mg/dL showed a strong correlation with hepatorenal dysfunction (Table 2), with 100% of patients exceeding this threshold having hepatorenal dysfunction, but only 20% of patients below this threshold showing the complication. At this cutoff, creatinine demonstrated perfect specificity (100%, 95% CI: 83.89-100) but limited sensitivity (83.33%, 95% CI: 66.44-92.66), with a negative predictive value of only 60% (95% CI: 60.87-91.14). In contrast, cystatin C >1.3 mg/L demonstrated perfect discrimination (Table 3), with all 30 patients exceeding this threshold having

hepatorenal dysfunction and all 20 patients below this threshold being free from this complication. This resulted in 100% sensitivity (95% CI: 88.65-100), 100% specificity (95% CI: 83.89-100), 100% positive predictive value (95% CI: 88.65-100), 100% negative predictive value (95% CI: 83.89-100), and 100% overall diagnostic accuracy (95% CI: 92.86-100). [Table 4]

Table 2: Association of Serum Creatinine with Hepatorenal Dysfunction

Serum Creatinine	HRD Present n (%)	HRD Absent n (%)	p-value
>2 mg/dL	25 (100)	0 (0)	<0.001
≤2 mg/dL	5 (20)	20 (80)	

HRD, hepatorenal dysfunction.

Table 3: Association of Cystatin C with Hepatorenal Dysfunction

Cystatin C	HRD Present n (%)	HRD Absent n (%)	p-value
>1.3 mg/L	30 (100)	0 (0)	<0.001
≤1.3 mg/L	0 (0)	20 (100)	

HRD, hepatorenal dysfunction.

Table 4: Comparative Diagnostic Performance of Biomarkers

Parameter	Serum Creatinine (>2 mg/dL)	Cystatin C (>1.3 mg/L)
Sensitivity, % (95% CI)	83.33 (66.44-92.66)	100 (88.65-100)
Specificity, % (95% CI)	100 (83.89-100)	100 (83.89-100)
PPV, % (95% CI)	100 (86.68-100)	100 (88.65-100)
NPV, % (95% CI)	60 (60.87-91.14)	100 (83.89-100)
Diagnostic accuracy, % (95% CI)	90 (78.64-95.65)	100 (92.86-100)

PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval.

ROC curve analysis confirmed the superior discriminatory ability of cystatin C (Figure 3). Serum creatinine achieved an AUC of 0.917 (95% CI: 0.827-1.000, p<0.001), indicating excellent discrimination, while cystatin C demonstrated near-perfect discrimination with an AUC of 0.997 (95% CI: 0.988-1.000, p<0.001) (Figure 3A). Similarly, when comparing eGFR-based estimates, cystatin C-based eGFR (AUC=0.968, 95% CI: 0.907-1.000) outperformed creatinine-based eGFR (AUC=0.937, 95% CI: 0.867-1.000), both with p<0.001 (Figure 3B). Moderate positive correlation was observed between serum creatinine and cystatin C (r=0.620, p<0.001), with stronger correlation between their respective eGFR estimates (r=0.818, p<0.001), indicating that both markers track similar underlying renal pathophysiology while maintaining complementary diagnostic utility.

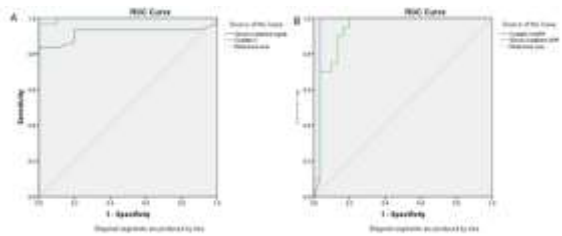

Figure 3. Receiver operating characteristic curves for hepatorenal dysfunction detection. (A) Serum biomarkers: Cystatin C (green line, AUC=0.997) demonstrated near-perfect discriminatory ability compared to serum creatinine (blue line, AUC=0.917) for identifying hepatorenal dysfunction. (B) eGFR-based estimates: Cystatin C-based eGFR (green line, AUC=0.968) outperformed creatinine-based eGFR (blue line, AUC=0.937), confirming superior diagnostic accuracy of cystatin C-derived estimates. Diagonal tan lines represent random chance (AUC=0.5).

The perfect diagnostic performance of cystatin C (100% sensitivity and specificity) at a cutoff of 1.3 mg/L establishes it as the superior biomarker for detecting hepatorenal dysfunction in patients with decompensated chronic liver disease. Our findings align with extensive international evidence demonstrating cystatin C's superior performance compared to creatinine-based methods. Markwardt et al. demonstrated that baseline cystatin C levels predict acute-on-chronic liver failure, hepatorenal syndrome, and 90-day mortality in patients with acutely decompensated cirrhosis, with patients in the highest cystatin C tertile having significantly worse outcomes ,[16] Kim et al. reported that cystatin C was independently associated with acute kidney injury development and progression in hospitalized patients with decompensated cirrhosis, with an optimal cutoff of 1.055 mg/L—remarkably similar to our 1.3 mg/L threshold.[17] A meta-analysis by Roos et al. encompassing multiple studies showed that cystatin C's diagnostic odds ratio (3.99; 95% CI: 3.41-4.57) significantly exceeded that of serum creatinine (2.79; 95% CI: 2.12-3.46) for predicting renal dysfunction, with cystatin C levels between 0.9-1.4 mg/L providing reliable exclusion of renal impairment when compared to gold-standard inulin-derived GFR measurements.18 Wang et al. in a Chinese cohort of cirrhotic patients found that cystatin C at a threshold of 1.24 mg/L achieved 87.6% sensitivity and 94.4% specificity, outperforming all creatinine-based methods including multiple eGFR equations.[19] The 16.67% of patients in our study who had hepatorenal dysfunction despite creatinine ≤2 mg/dL (false negatives for creatinine) highlights the clinical

significance of creatinine's limited sensitivity, as these patients would be missed by creatinine-based screening alone, potentially delaying critical interventions.

4. Clinical Implications and Future Directions

The clinical implications of these findings are substantial. Early and accurate detection of hepatorenal dysfunction enables: (1) timely initiation of albumin infusions and vasoconstrictor therapy (terlipressin, midodrine, or norepinephrine), which have been shown to improve renal function and short-term survival in hepatorenal syndrome; (2) appropriate medication dosing adjustments and avoidance of nephrotoxic agents such as aminoglycosides, NSAIDs, and iodinated contrast media; (3) identification of liver transplant candidates before development of irreversible renal damage, as early referral improves post-transplant outcomes; and (4) improved prognostic stratification for clinical decision-making and family counseling.[20,21] The 2012 KDIGO guidelines recommend cystatin C as a confirmatory test for GFR estimation when creatinine-based estimates fall between 45-60 mL/min/1.73m² without other signs of kidney damage—precisely the scenario commonly encountered in cirrhotic patients, where creatinine may be unreliable.[22] Integration of cystatin C into routine clinical assessment of decompensated cirrhosis patients would enable earlier intervention and potentially improve patient outcomes, though prospective randomized trials are needed to definitively demonstrate the impact on hard clinical endpoints such as mortality and transplant rates.

Despite its superior performance, several barriers limit widespread cystatin C adoption. These include higher cost compared to creatinine assays (approximately 5-10 times more expensive in most healthcare systems), limited clinician familiarity due to insufficient training in medical education curricula, absence of institutional protocols and clinical pathways incorporating cystatin C, poor integration into electronic health record systems where cystatin C results may not be prominently displayed or incorporated into decision support tools, and continued reliance on established creatinine-based workflows that have been standard practice for decades.[23] Addressing these barriers will require targeted educational initiatives for clinicians, cost-effectiveness analyses demonstrating long-term savings through improved outcomes and reduced complications, institutional guideline development supported by hepatology and nephrology societies, and enhanced electronic health record integration. However, the demonstrable diagnostic superiority and potential for improved patient outcomes strongly justify these efforts.

Study limitations warrant acknowledgment. The modest sample size (n=50) may limit generalizability and statistical power for subgroup analyses, though our findings are consistent with larger international studies. The cross-sectional design precludes assessment of longitudinal outcomes and temporal changes in biomarker levels following interventions. Gold-standard GFR measurement using inulin or iothalamate clearance was not performed, limiting definitive validation, though such measurements are rarely feasible in routine clinical practice. We did not comprehensively evaluate potential confounders of cystatin C levels, such as thyroid dysfunction, corticosteroid use, or systemic inflammation markers, though the consistent performance across diverse patient populations in multiple studies suggests these factors have minimal clinical impact. Single-center enrollment may limit applicability to populations with different etiology distributions or disease severity profiles. Despite these limitations, the robust performance of cystatin C in our cohort and its consistency with extensive international evidence support its clinical utility.

CONCLUSION

In conclusion, serum cystatin C at a cutoff of 1.3 mg/L provides highly accurate early detection of hepatorenal dysfunction in patients with decompensated chronic liver disease, with perfect diagnostic accuracy (100% sensitivity and specificity) significantly outperforming serum creatinine (83.33% sensitivity). The near-perfect discriminatory ability (AUC=0.997) and independence from confounding factors such as muscle mass and hepatic synthesis establish cystatin C as the preferred biomarker for renal function assessment in this population. Integration of cystatin C into routine clinical assessment protocols would enable earlier intervention, optimize risk stratification, guide therapeutic decision-making, and potentially improve patient outcomes. Future prospective studies evaluating the impact of cystatin C-guided management on mortality, liver transplant rates, and progression to hepatorenal syndrome are warranted to definitively establish its role in clinical algorithms for managing patients with decompensated cirrhosis.

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